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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/773,830	HUANG ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-4,8-26 and 28-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/19/01 and 09/03/2002 (2)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, claims 5-8 and 10-30, in Applicant's April 07, 2004 response. The traversal is on the ground(s) that the inventions are not independent or distinct because the peptides are connected in design, operation, and effect, and that the Examiner has not shown that a serious burden exist for searching all of peptides of Group II. This is not found persuasive because each of the disclosed peptides are patentable distinct from one another. This is so because of the uniqueness of each peptide. Although the peptides share a common non-chemical formula, the peptides do not share the same chemical structure. All of the peptides instantly claimed are unrelated to one another in chemical structure and function, and are therefore, are patentably distinct entities. Each sequence comprises completely different physical properties, such as chemical structure, primary sequence, evidenced by the different SEQ ID NO. assigned to each, stereochemistry, and molecular weight. Therefore, the activities, i.e. effects and function, of each unique peptide would be different. In addition, each peptide is non-obvious over each other. Thus, the peptides are independent and unique from one another.

It has been determined that each peptide sequence in are patentably distinct, a search for more than one of the specific and distinct sequences would pose an undue search burden for the Office. A divergent and non-overlapping search burden is required of Office because of the structural uniqueness of each sequence. Each SEQ ID NO. or permutation of each sequence must be searched independently of all others

in the patent and non-patent literature databases worldwide. This sequence search does not preclude a worldwide patent search under the appropriate classes and subclasses and cross-referencing indexes and a non-patent literature search for relevant terms.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claim(s)

2. Claims 1-44 are pending. Claims 1-4, 8-26 and 28-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Applicant's April 07, 2004 response. Claims 5-7, and 27 are currently under examination.

Specification

3. The disclosure is objected to because of the following informalities: Specification, lines 27-29, the symbols enclosed in the parenthetical notations, (), do not correspond with those that is depicted on Figure 1.

4. The instant specification contains several references to "Tables", however, no such item can be found within the disclosure.

Appropriate correction is required.

Claim Objections

5. Claim 5 objected to because of the following informalities:

Currently as written, it is unclear what is encompassed for the variable Y. It is recognized that Y can be OH, NH_2, OCH_3, $OCH_2C_6H_5$, or $NHCH_3$. However, currently

as written, it is unclear what is encompassed by the following clause: "Y can be from zero to nine amino acids". This also affects claims 6-7 and 27. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 5 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed a large number of amino acid sequences that have the following non-chemical formula:

$$X\text{-}R_1\text{-}R_2\text{-}R_3\text{-}R_4\text{-}R_5\text{-}R_6\text{-}R_7\text{-}R_8\text{-}R_9\text{-}R_{10}\text{-}R_{11}\text{-}R_{12}\text{-}R_{13}\text{-}R_{14}\text{-}R_{15}\text{-}R_{16}\text{-}R_{17}\text{-}R_{18}\text{-}R_{19}\text{-}R_{20}\text{-}R_{21}\text{-}Y$$

wherein Y, X, R_1-R_{21} are defined by alternatives.

The claims do not require that the peptides defined by the non-chemical formula to possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing features.

It is acknowledged that the specification teaches SEQ ID NO: 2, which is in agreement with the above non-chemical formula. The function of SEQ ID NO: 2 is

disclosed as: binding to CXCR4 but not CCR in a competitive binding assay, selectively inhibiting T-and dual-tropic HIV-1 entry in a cell to cell fusion assay that is describe on page 20 of the specification, and blocking the signaling and chemotaxis of SDF-1.

However, as currently written, the claims are drawn to a broad genus of peptides defined by the non-chemical formula. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a non-chemical formula. There is no identification of any particular portion of the non-chemical formula that must be conserved to perform the activities, noted above, of SEQ ID NO: 2. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Therefore, the peptide of SEQ ID NO: 2, but not the full breadth of the claim meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

8. Claims 5-7 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples,

(4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The following is an enablement analysis, based on Wands factors, for the peptides defined by the non-chemical formula. There are two aspects of the enablement analysis for the instantly claimed invention. The first is directed to the large number of peptides that is encompassed by the non-chemical formula that is recited claim 5. The other aspect of the enablement analysis is directed at SEQ ID NO: 2 and the pharmaceutical composition comprising the peptides defined by the non-chemical formula.

The claims are directed to a large number of peptides defined by the non-chemical formula recited in claim 5, wherein Y, X, and R_1-R_{21} are defined by alternatives. The claims also encompass a pharmaceutical composition comprising the peptides defined by the non-chemical formula. The claims are further limited to SEQ ID NO: 2. SEQ ID NO: 2 is derived from vMIP-II. vMIP-II is the viral macrophage inflammatory protein-II encoded by Kaposi's sarcoma-associated herpes virus. vMIP-II has been shown to have a broad-spectrum of interaction with both CC and CXC chemokine receptors including CCR5 and CXCR4, the two principal coreceptors for the cell entry of HIV-1.

The claims encompass an unreasonable number of inoperative peptides, which the skilled artisan would not know how to use. The skilled artisan would be unable to

make structural variants of the above generic formula that differ from SEQ ID NO: 2 because there is no teaching provided in the disclosure drawn to a commensurate number of peptides.

There are no working examples of peptides, other than SEQ ID NO: 2 that follow the above generic formula. From the working example, it was determined that SEQ ID NO: 2 have the following activities: binding to CXCR4 but not CCR in a competitive binding assay, selectively inhibiting T-and dual-tropic HIV-1 entry in a cell to cell fusion assay that is describe on page 20 of the specification, and blocking the signaling and chemotaxis of SDF-1. However, there is no guidance provided by Applicant for which structural variants could possess the above noted activities. There is no teaching in the specification on how to make peptides defined by the non-chemical formula that retains the listed activities. The claims are unduly broad because the non-chemical formula has no functional requirements. There is no indication that the species encompassed within the non-chemical formula would have the noted activities. Further, the skilled artisan would be unable to determine if a peptide possesses activities similar to SEQ ID NO: 2 simply by its non-chemical formula characteristics.

For these reasons, which include the complexity and unpredictability of the nature of the invention and lack of knowledge about function(s) of encompassed peptides related to SEQ ID NO: 2 by a non-chemical formula, the limited working examples of peptides defined by the non-chemical formula and its functions, the lack of direction or guidance for using peptides that are not identical to SEQ ID NO: 2, and the

breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Concerning the other aspect of the enablement analysis, SEQ ID NO: 2 and the pharmaceutical composition comprising the peptides defined by the non-chemical formula.

It is acknowledge that the specification suggests that SEQ ID NO: 2, which is in agreement with the non-chemical formula provided above, can be used to treat HIV-1 infection by inhibiting viral entry into cells expression the CXCR4 receptor (lines 24-27, page 21, specification), as preventative measure to avoid HIV infection, or as a therapeutic to treat patients already infected with HIV (lines 10-12, page 23, specification).

Therefore, it is determined that the nature of the invention is directed to peptides defined by the non-chemical formula and compositions thereof that interfere with HIV infection.

The breadth of the claims are directed to peptides defined by the non-chemical formula that prevents and treats HIV infection by inhibiting the initial HIV infection and replication of HIV virus by preventing viral entry into cells.

As mentioned above, the specification, including the working example(s), teaches that SEQ ID NO: 2 i) binds to CXCR4 but not CCR in a competitive binding assay, ii) selectively inhibits T-and dual-tropic HIV-1 entry in a cell to cell fusion assay that is described on page 20 of the specification, and iii) blocks the signaling and chemotaxis of SDF-1. While it is acknowledged that CXCR4 is one

of the two principal coreceptors for the entry of HIV, however it is unclear how the binding of SEQ ID NO: 2 to CXCR4 in the experimental protocol disclosed in the instant specification is indicative of HIV infection. The experimental protocol used by Applicant does not include HIV or other receptors that are necessary for HIV viral entry into cells. The experimental protocol that was used by Applicant is a competitive binding assay between CXCR4 and CCR5. In this assay, neither the virus nor other receptors that is necessary for HIV viral entry into cells is present. Thus, it is unclear how the binding of SEQ ID NO: 2 to CXCR4 is indicative of HIV infection.

Concerning the other teaching that is provided in the specification, SEQ ID NO: 2 selectively inhibits T- and dual-tropic HIV-1 entry. It is acknowledged that the specification disclosed that the assay used is a **cell-cell fusion assay** (emphasis added), however, it is unclear what the experimental protocol used in the cited assay was. Therefore, it is unclear how T- and dual-tropic HIV-1 entry is inhibited. Furthermore, it is unclear how the conclusion derived from such assay relates to HIV infection-- the treatment of HIV in HIV infected hosts, and the prevention of HIV in hosts that are vulnerable and susceptible to HIV infection.

Lastly, concerning the final teaching, SEQ ID NO: 2 blocks the signaling and chemotaxis of SDF-1 via CXCR4. From the disclosure in the specification, it is found that the above finding was made by measuring the intracellular calcium influx in Sup T1 cells expression the receptor. However, it is unclear how such

finding relates to HIV infection-- the treatment of HIV in HIV infected hosts, and the prevention of HIV in hosts that are vulnerable and susceptible to HIV infection. The experiment conducted does not involve the virus itself.

Furthermore, it is well known in the art that retroviral infections in general, and HIV infections in particular, are refractory to anti-viral therapies. The obstacles to HIV/AIDS therapy and vaccine formulations are well documented in the literature. The obstacles includes:

i) the inability current vaccine designs to elicit effective neutralizing antibodies against circulation strains of HIV[1, 2],

ii) the inability of current vaccine designs to prevent HIV from establishing persistent infection [3],

iii) the extensive global variability of HIV[4, 5, 6, 7, 8],

iv) the lack of understanding regarding the mechanisms of protection[9,10],

v) the lack of understating of which HIV antigens induce protective immunity and which immune effector mechanisms are responsible for protection[11],

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[1] Klausner et al. The need for a global HIV vaccine enterprise. Science, Vol. 300, June 2003, pp. 2036-2039, see underlined text.
[2] Desrosiers, Prospects for an AIDS vaccine. Nature Medicine, Vol. 10(3), March 2004, pp. 221-223, see underlined text.
[3] Ibid.
[4] Ibid.
[5] Nabel. Challenges and opportunities of development of an AIDS vaccine. Nature, Vol. 410, April 2001, pp. 1002-1007, see underlined text and Table 1.
[6] Desrosiers, opt. cit.
[7] Lee. Chapter 32 AIDS Vaccines: 32.1 Acquired immunodeficiency disease vaccines: design and development. AIDS: Biology, Diagnosis, Treatment, and Prevention, fourth edition, edited by DeVita, Jr. et al., Lippincott-Raven, 1997, pp. 605-616, see underlined text on page 609.
[8] Bende, et al. Update: Search for an AIDS vaccine. AIDS Read, 10(9), 2000, pp. 526-537, see Table 3.
[9] Klausner, op. cit.
[10] Desrosiers, op. cit
[11] Ibid.

vi) lack of immune correlates[12, 13, 14, 15],

vii) it is unknown if strong immune responses at muscosal surfaces will be necessary to provide protection from sexual transmission[16],

viii) inability to identify immunogens that induce broad and long lasting immunity[17], and

ix) lack of a practical animal model system for HIV. [18, 19,20,21, 22].

The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the instantly claimed invention with a reasonable expectation of success and without undue experimentation.

Furthermore, Applicant has not provided any convincing evidence that SEQ ID NO: 2 or that any peptides defined by the non-chemical formula and a pharmaceutical composition thereof is indeed therapeutic against HIV infection. There is no working example that is drawn to the administration of peptides defined by the non-chemical formula. Nor is there an indication for what kind of immune response would be generated by peptides defined by the non-chemical formula, and when the administration should start and end or how much would be effective or sufficient. In

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[12] Nabel, op. cit.
[13] Beyrer, The HIV/AIDS vaccine research effort: An update. The Johns Hopkins University AIDS Service, The Hopkins HIV Report, Vol. 15 (1), January 2003, pp. 1-16, see pp. 6-7 and underlined text.
[14] Lee, op. cit., p. 608.
[15] Bende, op. cit.
[16] Ibid.
[17] Nable, op. cit.
[18] Feinberg et al. AIDS vaccine models: challenging challenge viruses. Nature Medicine, Vol 8 (3), March 2002, pp 207-210, see underlined text.
[19] Nabel, op. cit.
[20] Beyrer, op. cit.
[21] Lee, op. cit., p. 609.
[22] Bende, op. cit.

addition, there is no teaching in the art concerning peptides defined by the non-chemical formula and the administration of said peptides to HIV infected subjects as a pharmaceutical composition against HIV infection. Additionally, there is no teaching for what type of biological effects the instantly claimed peptide would generate upon the administration of said peptide. And if an immune response is observed, there is no teaching in the specification whether the immune response generated would be sufficient to treat and/or prevent HIV infection.

Therefore, the disclosure in the specification does not contain sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Therefore, in view of the above enablement analysis, one skilled in the art would not be able to practice the instantly claimed invention with a reasonable expectation of success without an undue burden of experimentation.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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